



# Development of an Aggressive Treatment Protocol against Neonatal Calf Diarrhea: The Last Chance to Rescue Severely Infected Calves

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## ABSTRACT

Despite many efforts to control and treat neonatal calf diarrhea (NCD), it remains the primary cause of calf mortality in dairy herds worldwide. The objective of this article was to develop and discuss an empirical therapeutic protocol to save newborn calves with severe diarrhea. The pathophysiology of diarrhea has been well described previously. However, there is a significant gap between scientific findings and practical implementations. Reducing the number of calves with failure of passive transfer, regular sanitation of the calf environment, and optimal dry cow nutrition and management are fundamental measures in controlling diarrhea in commercial settings. As such, optimizing colostrum feeding management and improving ambient hygiene are among the most important management practices to prevent calf diarrhea. Nonetheless, the occurrence of NCD would be unavoidable due to its multifactorial nature and pathophysiology. According to the degree of dehydration and general appearance of ill calves (e.g., degree of sunken eye and loss of suck reflex), NCD can be classified into mild to severe cases. Early diagnosis and treatment of both mild and severe cases could reduce pathogens shedding into the calf environment. Notably, diarrhea treatment needs profound scientific farm education and mentoring regarding the physiology of NCD. Since a variety of organisms, such as bacteria, viruses, and protozoa, may be responsible for NCD, it is evident that reliable diagnosis requires optimal sampling and laboratory analysis. However, waiting for laboratory results may waste the golden time of treatment. Therefore, rapid and decisive treatment would be mandatory, especially in severely infected calves or sepsis cases. Accordingly, an effective aggressive treatment protocol was developed and discussed in this article as the last chance to keep diarrheic calves alive.

**Keywords:** Aggressive treatment, Calf diarrhea, Dairy calf, Farm Management, Prevention

## INTRODUCTION

Diarrhea and other digestive tract disorders account for the most important factors causing calf mortality worldwide (Zhang et al., 2019). The importance of calf health and well-being has been described over the last decade from short-term (calf loss and veterinary cost) and long-term (herd future productivity) perspectives (Lorenz, 2021). Enhancing the health of newborn calves by optimizing management factors such as colostrum feeding and welfare, and early diagnosis and treatment of ill calves can significantly enhance herd productivity and longevity. After birth, as newborn calves adapt to the new extra-uterine environment, they are exposed to a variety of harmful pathogens (Malmuthuge and Guan, 2017). Importantly, however, the immune system of neonatal calves is still not fully developed. Newborn calves depend almost totally on maternal colostrum ingestion to acquire immunity (Nikkhah and Alimirzaei, 2021). As such, the balance between host immunity and environmental contaminations determines calf susceptibility to infectious diseases such as diarrhea. Diarrheic calves and even those recovered from diarrhea shed infectious agents into the surroundings and are considered as main contaminators. Therefore, early diagnosis and effective treatment are vital for saving diarrheic calves.

As noted, many pathogenic organisms are responsible for severe diarrhea in neonatal calves. Bacteria including enterotoxigenic *E. coli* (ETEC), and *salmonella enterica*, *salmonella dublin*, *salmonella typhimurium*; viruses such as *rotavirus* and *coronavirus*; and protozoa such as *cryptosporidium parvum* are amongst the most important pathogenic organisms that can infect young calves and causes mortality (Cho and Yoon, 2014). Independent of the type of pathogens involved in the etiology of diarrhea, clinical symptoms are usually similar, thus making specific diagnoses difficult. Watery feces, lethargy, anorexia, dehydration, and loss of suckling behavior are common signs in all types of diarrheas. However, because of the importance of immediate interventions to save ill calves, the type of diarrhea should

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be known. The age at which calves are infected and the score of feces can help veterinarians and clinicians infer the principal cause of diarrhea. Hence, they can decide how to deal with an ill calf. For instance, ETEC can infect neonatal calves during 2-4 days of age and cause watery diarrhea. *Salmonella spp.* infection can also be diagnosed with mucoid-bloody diarrhea in calves younger than 3 weeks of age (Cho and Yoon, 2014). In case of viruses, in calves younger than 3 weeks of age, watery-pale-yellowish diarrhea can be considered as viral diarrhea (Gomez and Weese, 2017). As viruses invade mature intestinal villi, nutrient malabsorption results in prolonged diarrheic days and calf weakness (Cho and Yoon, 2014). It is important to note that calf excretions should be sampled carefully to avoid environmental contaminations and sent to the laboratory for accurate diagnosis. Laboratory testing is needed for making right management decisions and developing long-term preventive protocols.

As described previously (Nikkhah and Alimirzaei, 2021), mild cases of diarrhea (feces not very watery with calves being able to stand and suckle) can be treated successfully by the administration of oral fluid electrolytes and related appropriate therapies. However, in severe cases, the scenario is totally different. The severely infected calves lose considerable volumes of water and electrolytes (e.g., sodium, potassium, chloride, and bicarbonate), making calves highly dehydrated, known by sunken eyes. It appears that fluid loss during severe diarrhea would exceed the farm staff's imaginations and expectations. Water loss in calves with severe diarrhea can range from 13-18% (or even greater) of body weight daily (Berchtold, 2009). Knowing that approximately 75% of calf body weight consists of water, a diarrheic calf with 40 kg body weight may lose about 6 lit/d water (Naylor, 2009). Underestimating water and electrolyte requirements of diarrheic calves is one of the most important reasons for calf mortality in dairy herds. In addition, severely diarrheic calves may develop metabolic acidosis, which may lead to central nervous system malfunction, failure of suckling behavior, recumbency, coma, and death (Berchtold, 2009). Therefore, correcting metabolic acidosis is vital for calf survival. Since an immediate intervention is required for successful treatment, the following practical protocol is recommended for on-farm use.

## PROTOCOL PRESENTATION

Intravenous (IV) fluid therapy must be used in severe cases (recumbent cases with sunken eyes) to replace the lost water and electrolytes to restore extracellular and plasma fluid volumes (Naylor, 2009). The amount of fluid needed in the first injection is totally dependent on the dehydration rate and general wellness of the ill calf (Berchtold, 2009; Constable et al., 2021). However, as a practical guideline, 2-4 liters of dextrose-saline serum (5% dextrose, 0.9% saline) must be injected immediately. As noted above, in severe cases, water loss may be more than expected; thus, the second and third IV injections may be needed. Two liters of isotonic dextrose-saline serum is recommended every 5 or 6 hours. The isotonic serum is used to maintain the balance between blood sugar and electrolytes (Naylor, 2009). The IV injections should be stopped when the suckling reflex is recovered, and the calf is able to stand easily. After that, IV fluid therapy could be replaced by oral fluid therapy (Constable et al., 2021). Usually, systemic inflammation occurs in heavily infected calves or those with septicemia (Constable et al., 2021), leading to organ failure and death. Consequently, alleviating inflammatory responses should be considered the second step in treating severe cases of diarrhea. Hypertonic saline solution (7.2%) is useful for alleviating inflammatory responses and increases plasma volume and cardiac output (Constable et al., 2021). Thus, it should be administered for about 300-400 ml in the first injection combined with an isotonic dextrose-saline solution. According to the authors' extensive farm experience, adding 1-3 ml of anti-inflammatory drugs, such as dexamethasone, meloxicam, or flunixin meglumine into the first injection solution can contribute to mitigating unwanted severe anti-inflammatory responses and could help the calf resume optimal organ's function. Moreover, eliminating the infectious agent, especially in sepsis cases would be essential. As such, IV administration of antibiotics accompanied by anti-inflammatory drugs is necessary for eliminating bacterial agents responsible for diarrhea (Berchtold, 2009). In severe cases, antibiotics use can be replicated every 12 hours. With regard to herd's veterinarian recommendation, antibiotics, such as ceftriaxone, gentamicin, or marbofloxacin must be added to the first injection solution. It is also important to note that serum solutions are usually prepared and presented in 1-liter containers; thus, anti-inflammatory drugs and antibiotics could be gradually added to the second container. Alongside drug administration, adding 500 ml of isotonic sodium bicarbonate or 100 ml of hypertonic sodium bicarbonate is needed for correcting acidosis. All the above procedures must be performed in the first injection time (immediately after diagnosing severe diarrhea). In the second or third injections, isotonic dextrose-saline solution would be enough for the rehydration of affected calves. Vitamins, including B-complex, would be highly recommended because calves with severe diarrhea are almost energy-deficit (Berchtold, 2009). Administration of B-group vitamins can fuel energy-releasing pathways and thereby help calves recover rapidly. Fat-soluble vitamins (A, D<sub>3</sub>, and E) are also recommended because of their effects on repairing mucosal membranes during bacterial or viral invasion (Constable et al., 2021). The above drugs and materials should be administered 5 consecutive days to ensure bacterial elimination. Antibiotics and anti-inflammatory drugs can help prevent secondary bacterial infection in viral diarrhea cases.

Given the above-mentioned fluid and antibiotics-drug therapies, optimal nursing is an important factor in determining calf survival. All in all, although aggressive treatment would be the last chance to save sepsis or heavily infected and diarrheic calves, it might not be effective in all cases because of individual pathophysiological differences among calves.

## CONCLUSION

Neonatal calf diarrhea can be fatal if the disease is not detected early enough and goes forward to induce sepsis. In severe cases, early intervention is vital for rescuing affected calves. Therefore, aggressive treatment would be needed to recover calves from deadly infection status. Administration of normal and hypertonic saline serum and sodium bicarbonate is fundamental to return lost water and electrolytes as well as to correct metabolic acidosis. Intravenous therapy should be continued with isotonic serum until calf recovery from the risk point. Aggressive treatment, as developed and presented here, would be the last chance to save highly infected calves. It is necessary to note that individual calf differences in resistance to disease is a determining factor in their full or partial recovery. Thus, aggressive treatment might not be necessarily successful in all cases.

## DECLARATIONS

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### Authors' contribution

The authors' contribution to this work was equal. The tasks included idea conceptualization, strategic development and contemplation, and manuscript writing and editing. The final draft of the manuscript was checked by all authors.

### Competing interests

None.

### Ethical considerations

The authors have made necessary ethical considerations (e.g., plagiarism, consent to publish, misconduct, data fabrication and/or falsification, double publication and/or submission, and redundancy).

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